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LaRosa

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(54) **ANTI-CCR2 ANTIBODIES AND METHODS OF USE THEREFOR**

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(58) **Field of Classification Search** None
See application file for complete search history.

(56) **References Cited**

U.S. PATENT DOCUMENTS

4,816,397 A	3/1989	Boss et al.
4,816,567 A	3/1989	Cabilly et al.
5,225,539 A	7/1993	Winter
5,440,021 A	8/1995	Chunthanapai et al.
5,543,503 A	8/1996	Chunthanapai et al.
5,571,713 A	11/1996	Lyle et al.
5,585,089 A	12/1996	Queen et al.
5,657,277 A	8/1997	Shirley
5,693,761 A	12/1997	Queen et al.
5,693,762 A	12/1997	Queen et al.
5,707,815 A	1/1998	Charo et al.
5,808,960 A	9/1998	McClure
5,858,089 A *	1/1999	Martonovic
5,859,205 A	1/1999	Adair et al.
5,985,279 A	11/1999	Waldmann et al.
6,006,339 A	12/1999	McClure
6,075,181 A *	6/2000	Kucherlapati et al.
6,084,075 A *	7/2000	Lind et al.
6,312,689 B1	11/2001	LaRosa
6,352,832 B1	3/2002	LaRosa et al.
6,395,497 B1	5/2002	LaRosa
6,406,694 B1	6/2002	LaRosa
6,406,865 B2	6/2002	LaRosa
6,448,021 B1	9/2002	LaRosa
6,451,522 B2	9/2002	LaRosa
6,458,353 B1	10/2002	LaRosa
6,491,915 B2	12/2002	LaRosa

6,696,550 B2	2/2004	LaRosa et al.
7,053,202 B2	5/2006	O'Keefe et al.
2003/0165494 A1	9/2003	LaRosa et al.
2004/0126851 A1	7/2004	LaRosa et al.
2004/0132980 A1	7/2004	LaRosa et al.
2004/0151721 A1	8/2004	O'Keefe et al.
2004/0265303 A1	12/2004	LaRosa et al.
2006/0147445 A1	7/2006	O'Keefe et al.

FOREIGN PATENT DOCUMENTS

WO	WO 91/09967	7/1991
WO	WO 94/09128	4/1994
WO	WO 94/12214	6/1994
WO	WO 95/08576	3/1995
WO	WO 95/19436	7/1995
WO	WO 97/19499	* 9/1997
WO	WO 97/47319	12/1997
WO	WO 98/42360	10/1998
WO	WO 98/44953	10/1998
WO	WO 99/15666	4/1999
WO	WO 00/05265	2/2000

OTHER PUBLICATIONS

Lederman et al. Molecular Immunology. 1991. 28(11):1171-1181.
Li et al. PNAS. 1980. 77(6):3211-3214.*
Frade et al. The Journal of Immunology 1997, 159:5576-5584.*
Li et al. Biochemistry 2000, 39:6296-6309.*
Förster, R., et al., "A general method for screening mAbs specific for G-protein coupled receptors as exemplified by using epoxide tagged BLR1-transfected 293 cells and solid-phase cell ELISA," *Biochemical and Biophysical Research Communications*, 196(3):1496-1503 (1993).

Boring, L., et al., "Decreased lesion formation in CCR2^{-/-} mice reveals a role for chemokines in the initiation of atherosclerosis," *Nature*, 394(27):894-897 (1998).

Ylä-Herttula, S., et al., "Expression of monocyte chemoattractant protein 1 in macrophage-rich areas of human and rabbit atherosclerotic lesions," *Proc. Natl. Acad. Sci.*, USA, 88:5252-5256 (1991).

Taubman, M.B., et al., "JE mRNA Accumulates Rapidly in Aortic Injury and in Platlet-Derived Growth Factor-Stimulated Vascular Smooth Muscle Cells," *Circulation Research* 70(2): 314-325 (1992).

Feng, A., et al., "Red Wine Inhibits Monocyte Chemoatactic Protein-1 Expression and Modestly Reduces Neointimal Hyperplasia After Balloon Injury in Cholesterol-Fed Rabbits," *Circulation* 100:2254-2259 (1999).

(Continued)

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(57) **ABSTRACT**

The present invention relates to an antibody or functional fragment thereof which binds to a mammalian (e.g., human) CC-chemokine receptor 2 (CCR2) or a portion of the receptor and blocks binding of a ligand to the receptor. The invention further relates to a method of inhibiting the interaction of a cell bearing mammalian CCR2 with a ligand thereof, and to use of the antibodies and fragments in therapeutic, prophylactic and diagnostic methods.